Citation:

Oh K, Hu FB, Cho E, Rexrode KM, Stampfer MJ, Manson JE, Liu S, Willett WC. Carbohydrate intake, glycemic index, glycemic load and dietary fiber in relation to risk of stroke in women. *Am J Epidemiol.* 2005 Jan 15; 161 (2): 161-169.

PubMed ID: 15632266

Study Design:

Prospective cohort study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the associations of dietary carbohydrate, glycemic index, and glycemic load with stroke risk.

Inclusion Criteria:

Nurses' Health Study participants: 121,700 female registered nurses aged 30-55 years completed a mailed questionnaire about their lifestyle factors and medical history, including previous cardiovascular disease (CVD) cancer, diabetes, hypertension (HTN) and high blood cholesterol levels.

Exclusion Criteria:

- Women who left 10 or more food items blank on the questionnaire or who had an implausible total energy intake
- Women who had a history of CVD (angina, myocardial infarction, stroke, other CVD, N=1,645), cancer (N=3,610), diabetes (N=1,410) or hypercholesterolemia (N=4,269) before June 1980.

Description of Study Protocol:

Recruitment

- The Nurses' Health Study was initiated in 1976 when 121,700 female registered nurses aged 30-55 years completed a mailed questionnaire about their lifestyle factors and medical history, including previous CVD, cancer, diabetes, hypertension and high blood cholesterol levels
- Every two years, follow-up questionnaires are sent to the participants.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- Dietary intake measured with semi-quantitative 61-item food-frequency questionnaire (FFQ) (expanded to 116 items in 1984)
- Average daily intake of nutrients, glycemic index and glycemic load calculated.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- For each study participant, person-years of follow-up were counted from the date and stroke diagnosis, the date of death, or June 1, 1998, whichever came first
- Women were grouped in quintiles of CHO intake, dietary glycemic index and dietary glycemic load
- In multivariate analysis, the estimated relative risks were simultaneously adjusted for potential confounding variables by using Cox proportional hazards regression
- To best represent the participants' long-term dietary pattern during follow-up, a cumulative average method was used
- Analyses were also stratified by BMI
- Tests for trends were conducted by assigning the median value to each quintile and modeling these values as a continuous variable
- The log-likelihood ratio test was used to assess the significance of interaction terms.

Data Collection Summary:

Timing of Measurements

- The Nurses' Health Study was initiated in 1976
- Every two years, follow-up questionnaires are sent to the participants
- Information on usual diet collected in 1980, 1984, 1986, 1990 and 1994
- 18-year follow-up from 1980 to June 1, 1998.

Dependent Variables

- Incident stroke; women who reported stroke on a follow-up questionnaire were asked for permission to review their medical records. Medical records were available for 74% of stroke cases and were reviewed by physicians without knowledge of the participant's exposure status
- Deaths were ascertained by reports from relatives or postal authorities and a search of the National Death Index, mortality follow-up was more than 98% complete
- Strokes were sub-classified into ischemic and hemorrhgic according to Perth Community Stroke Study criteria and based on computed tomography, MRI or autopsy findings

Independent Variables

- Dietary intake measured with semi-quantitative 61-item FFQ (expanded to 116 items in 1984)
- Average daily intake of nutrients, glycemic index and glycemic load calculated.

Control Variables

- Age
- BMI
- Smoking
- Alcohol intake
- Parental history of myocardial infarction
- Histories of hypertension, hypercholesterolemia and diabetes
- Postmenopausal hormone use
- Aspirin use
- Multivitamin use
- Vitamin E supplement use
- Physical activity
- Energy intake
- Cereal fiber intake.

Description of Actual Data Sample:

- *Initial N:* 78,779 women followed for 18 years
- *Attrition (final N):* 78,779 women
- *Mean age:* 46±7 years at baseline
- *Ethnicity:* Not mentioned
- *Other relevant demographics:* Not applicable
- *Anthropometrics:* Not applicable
- *Location:* United States.

Summary of Results:

Relative Risks of Stroke According to BMI and Total Carbohydrate Intake, Dietary Glycemic Index and Dietary Glycemic Load Among 78,779 Female Nurses from 1980 to 1998

Variables	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
Carbohydrate intake						
Total stroke, <25kg/m^2 (N=528)	1	0.94	0.80	0.89	0.89	0.54
Total stroke, >25 kg/m^2 (N=492)	1	1.15	1.50	1.63	2.13	0.002
Ischemic stroke, <25kg/m^2 (N=259)	1	0.84	0.53	0.54	0.58	0.05

Ischemic stroke, >25kg/m^2 (N=256)	1	0.92	1.39	1.20	1.61	0.16
Hemorrhagic stroke, <25kg/m^2 (N=178)	1	1.36	1.71	1.54	1.57	0.20
Hemorrhagic stroke, >25kg/m^2 (N=101)	1	2.37	2.17	3.50	3.84	0.02
Glycemic Index						
Total stroke, <25kg/m^2 (N=528)	1	0.80	0.77	0.76	0.90	0.37
Total stroke, >25kg/m^2 (N=492)	1	0.94	1.03	1.11	1.12	0.26
Ischemic stroke, <25kg/m^2 (N=259)	1	0.73	0.94	0.73	0.84	0.42
Ischemic stroke, >25kg/m^2 (N=256)	1	1.09	1.06	1.29	1.39	0.09
Hemorrhagic stroke, <25kg/m^2 (N=178)	1	0.72	0.53	0.71	0.98	0.87
Hemorrhagic stroke,>25kg/m^2 (N=101)	1	1.53	1.89	1.41	1.27	0.54
Glycemic load						
Total stroke, <25kg/m^2 (N=528)	1	1.04	0.81	0.97	1.03	0.93
Total stroke, >25kg/m^2 (N=492)	1	1.33	1.15	1.42	1.61	0.01
Ischemic stroke, <25kg/m^2 (N=259)	1	1.00	0.73	0.72	0.88	0.42
Ischemic stroke, >25kg/m^2 (N=256)	1	1.37	1.13	1.27	1.56	0.11
Hemorrhagic stroke, <25kg/m^2 (N=178)	1	1.36	1.20	1.35	1.07	0.81
Hemorrhagic stroke, >25kg/m^2 (N=101)	1	1.49	1.57	2.00	1.69	0.13

Key Findings

- During an 18-year follow-up, 1,020 stroke cases were documented (including 515 ischemic and 279 hemorrhagic, the rest could not be confirmed)
- In analyses adjusting for non-dietary risk factors and cereal fiber, CHO intake was associated with elevated risk of hemorrhagic stroke when the extreme quintiles were compared (RR=2.05, 95% CI: 1.10-3.83, P for trend=0.02), but not with ischemic stroke
- The positive association between CHO intake and stroke risk was most evident among

women with a BMI>25kg/m^2
- Dietary glycemic load was positively associated with total stroke among those women whose BMI was >25kg/m^2 (RR=1.61, 95% CI: 1.15-2.27, P for trend=0.01) but associations for type of stroke were not statistically significant
- Dietary glycemic index was not related to risks of total stroke or type of stroke within BMI categories
- Cereal fiber intake was inversely associated with total and hemorrhagic stroke risk; for total stroke, RR=0.66 (95% CI: 0.52-0.83, P for trend=0.001) and for hemorrhagic stroke, RR=0.51 (95% CI: 0.33-0.78, P for trend=0.01)
- Intake of fiber from fruits and vegetables was not associated with risks of total stroke or type of stroke.

Author Conclusion:

- In summary, these results provide evidence that high intake of refined CHO may increase risk of hemorrhagic stroke in women and that the deleterious effect is stronger among those who are overweight or obese. In addition, the data support a benefit of cereal fiber in preventing hemorrhagic stroke
- These findings suggest that replacing sugar and refined starches with whole-grain, high-fiber forms of CHO may reduce hemorrhagic stroke, particularly among women who are overweightor obese
- Furthermore, our results may have implications for preventing hemorrhagic stroke in Asian countries with a higher rate of hemorrhagic stroke and a higher intake of CHO.

Reviewer Comments:

- *18-year follow-up and dietary intake measured several times during that period; controlled for many factors.*

Authors note the following limitations:

- *Possibility of residual confounding by unknown risk factors could not be excluded*
- *Error in assessing dietary intake is inevitable*
- *Blood lipid levels not measured.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes

4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes

4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes